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Dated: 9/17/02

Signature: (Anna P. Lucey)

Docket No.: CIBT-P01-119
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Group Art Unit: 1646

Examiner: Not Yet Assig

In re Patent Application of:

Ling et al.

Application No.: 09/883848

Filed: June 18, 2001

For: ANGIOGENESIS-MODULATING

COMPOSITIONS AND USES

INFORMATION DISCLOSURE STATEMENT (IDS)

Commissioner for Patents Washington, DC 20231

Pursuant to 37 CFR 1.56, the attention of the Patent and Trademark Office is hereby directed to the references listed on the attached PTO/SB/08. It is respectfully requested that the information be expressly considered during the prosecution of this application, and that the references be made of record therein and appear among the "References Cited" on any patent to issue therefrom.

This Information Disclosure Statement is filed before the mailing date of a first Office Action on the merits as far as is known to the undersigned.

A copy of each reference on PTO/SB/08 is attached.

While the information and references disclosed in this Information Disclosure Statement may be "material" pursuant to 37 CFR 1.56, it is not intended to constitute an admission that any patent, publication or other information referred to therein is "prior art" for this invention unless specifically designated as such.

SEP 2 3 2002 CENTER 1600/00 Application No.: 09/883848 Docket No.: CIBT-P01-119

In accordance with 37 CFR 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information as defined in 37 CFR 1.56(a) exists. It is submitted that the Information Disclosure Statement is in compliance with 37 CFR 1.98 and the Examiner is respectfully requested to consider the listed references.

Dated:

Respectfully submitted,

David P. Halstead, Ph.D. Registration No.: 44,735

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Agent for Applicants

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·	AA	WO 95/18856	7/13/9	95	PCT			8	
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	AD	WO 00/25725	5/11/0	00	PCT				
	AE	WO 00/41545	7/20/0	00	PCT				
	AF	WO 00/74706	12/14/	00	PCT				
····	AG	WO 01/19800 A2	3/22/0	01	PCT				
	АН	WO 01/26644 A2	4/19/0	01	PCT				
	AI	WO 01/74344 A2	10/11/	01	PCT				
				JMENTS			or, Title, Date, Pertine		
	AJ	Apelqvist, A. et al. 7, 801-804 (1 Oct. 1		lgehog dir	rects specialized mesoderm diff	ferentiation in the	e intestine and pancres	s. Curren	it Biology
	AK	Asahara, T. et al. Ti neovascularization.			s, angiopoietin-1 and angiopoie 240 (1997).	tin-2, modulate	VEGF-Induced postna	tal	
	AL	Ballara, S. C. et al. Path. 80, 235-250 (1		els, new a	npproaches: angiogenesis as a t	herapeutic target	in musculoskeletal di	sorders. II	nt. J. Exp.
1	AM				hancement of collateral blood (2183-2189 (May 1994).	flow to ischemic	myocardium by vascu	lar endoth	elial
	AN	Battler, A. et al. Into J. Am. Coll Cardiol.			n of basic fibroblast growth facec. 1993).	tor enhances ang	iogenesis in infracted	swine my	ocardium.
	АО	Beck, L. Jr. & D'An	nore, P. A	Vascula	ar development: cellular and m	nolecular regulati	on. <i>FASEB J</i> . 11, 365	-373 (Apr	il 1997).
	AP	Bitgood, M. J. & Mo mouse embryo. Dev			Igehog and Bmp genes are coex 8 (Nov. 1995).	xpressed at many	diverse sites of cell-c	ell interac	tion in the

D DDO (01	2/00		I B 1 (1) 1 40 (1) 15	Sheet Page	e 2 of 6			
Form PTO/SI			Docket Number (Optional)	Application Number				
		DISCLOSURE CITATION	CIBT-P01-119	09/883,848				
		APPLICATION	Applicant	•				
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CIME	\		Filing Date	Group Art Unit	_			
	M —		June 18, 2001	1646				
SEP 2:0 2002				ates the male germline. Curr. Biol. 6, 298-00 (1996)				
PRADEMA	AR		endothelial cell stimulating angiogene Dermatol. 141, 1054-1060 (Dec. 1994)	esis factor and vascular endothelial growth actor are 200	:IVE			
٧.	AS	Buschmann & Schaper, W. 7 2000).	The pathophysiology of the collateral c	irculation (arteriogenesis). J. Pathol. 190, 8-342 (Feb.				
	ΑТ	Carpenter, D. et al. Character 13634 (10 Nov. 1998).	rization of two patched receptors for the	e vertebrate hedgehog protein family. PNAS 95, 13630)-			
	AU	Chiang, C. et al. Cyclopia an (1996).	d defective axial patterning in mice lac	king sonic hedgehog gene function. Nature 383, 407-4	13			
	AV	Cherrington, J. M. et al. New 1-38 (2000).	paradigms for the treatment of cancer	the role of anti-angiogenesis agents. Adv. Cancer Res	. 79,			
	AW	Couffinhal, T. et al. Impaired factor in ApoE-/- mice. Circu		ted with reduced expression of vascular endothelial gro	wth			
	AX	D'Amato. Angiogenesis Inhi	bition in Age-related Macular Degene	ration. Opthamology 102, 1261-1262 (Sept. 1995).				
	AY	Ding, Q. et al. Mouse suppre distribution of Gli 1. Curr. B.		sonic hedgehog signaling and alters the subcellular				
	AZ	Dockter, J. L. Sclertome indu	action and differentiation. Curr. Top I	Dev Biol. 48, 77-127 (2000).				
	ВА	Dodd, J. et al. The when and	where of floor plate induction. Science	e 282, 1654-1657 (1998).				
	BB	Ericson, J. et al. Graded sonic hedgehog signaling and the specification of cell fate in the ventral neural tube. Cold Spring Harbor Symp. Quant. Biol. 62, 451-466 (1997).						
-	ВС	Ericson, J. et al. Sonic hedge. Dev. Biol. 39, 809-816 (1995)		rning along the rostrocaudal axis of the neural tube. In	t. J.			
Ų	BD	Engler, D. A. Use of vascular endothelial growth factor for therapeutic angiogenesis. Circulation 94, 1496-1498 (1 Oct. 1996).						
	BE		gged proteins detected with the 9E10 a analysis. <i>Biochem. Cell Biol.</i> 76, 125	ntibody in immunofluorescence and immunoprecipitati -128 (1998).	on			
	BF	Folkman, J. & Shing, Y. Ang	iogenesis. J. Biol. Chem. 267, 10931-	10934 (5 June 1992).				
	BG			ne vascular endothelial growth factor receptor (Flk-1/KI) owth of multiple tumor types. Cancer Res. 59, 99-106 (

				Sheet Page 3 of 6			
Form PTO/SI			Docket Number (Optional)	Application Number			
		DISCLOSURE CITATION `	CIBT-P01-119	09/883,848			
		APPLICATION	Applicant				
IPE (Use	e severa	l sheets if necessary)	Ling et al.				
$D \cap \mathcal{E} \nearrow$			Filing Date	Group Art Unit			
70	}		June 18, 2001	1646			
	} \	Goodrich, L. V. et al. Altered	neural cell fate and medulloblastoma in mou				
P 2 0 2802	BH			男 % 四			
<u> </u>	/ /						
49	f	Hammerschmidt, M. et al. Th	e world according to hedgehog. TIG. 13, 14	-21 (Jan. 1997).			
TRADEMAN	ВІ			-21 (Jan. 1997).			
,							
		Harada V et al Basic fibrob	last growth factor improves myocardial func	tion in chronically ischemic porcine hearts. J. Clin.			
	D.	Invest. 94, 623-630 (Aug. 199		non in emonically ischemic potenic nears. 5. cim.			
\ \	BJ	Invest. 77, 025-030 (Mug. 1777).					
			· · · · · · · · · · · · · · · · · · ·				
				nomously induces multiple ventral cell types. Nat.			
	BK	Neurosci. 3, 41-46 (Jan. 2000)).				
		Ingham, P.W. Signaling by he	edgehog family proteins in Drosophila and v	ertebrate development. Curr. Opin. Genet. Dev. 5,			
	BL	492-498 (1995).		•			
	ļ	Isner I M et al Arterial gen	e transfer for therapeutic angiogenesis in nat	ients with peripheral artery disease. Hum. Gene Ther.			
	BM	7, 959-988 (20 May 1996).	e danster for dierapeatre anglogenesis in par	tends with peripheral artery disease. Trum. Some There			
	DIVI	,, ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,					
		Iwamoto, M. et al. Actions of	hedgehog proteins on skeletal cells. Crit. R	ev. Oral Biol. Med. 10, 477-486 (1999).			
	BN	ļ					
			A. Expression of Sonic hedgehog and its put	ative role as a precursor cell mitogen in the			
	ВО	developing mouse retina. Dev	velop. 124, 363-371 (Jan. 1997).				
		Johnson, R. L. & Tabin, C. J.	Molecular models for vertebrate limb development	opment, Cell 90, 979-990 (1997).			
	BP	,					
· ·		Karasek M A Progress in o	ur understanding of the biology of psoriasis.	Cutic 64 319-322 (Nov. 1999)			
	BQ	Karasek, W. A. Trogress in o	at understanding of the biology of psortasis.	Calls. 04, 517-322 (1104. 1777).			
	ÞŲ						
				 			
		Karp, S. J. et al. Indian hedge	thog coordinates endochondral bone growth	and morphogenesis via parathyroid hormone related-			
	BR	protein-dependent and -indep	endent pathways. Devel. 127, 543-548 (2000)	<i>)</i>).			
		Kenyon, B. M. et al. A model	of angiogenesis in the mouse cornea. Inves	t. Opthamol. Vis. Sci. 37, 1625-1632 (1996).			
	BS						
		Klagsbrun, M. & D'Amore, P	. A. Regulators of angiogenesis. Annu. Rev.	Physiol 53 217-239 (1991)			
	BT						
•	5.						
	ļ	Vloha W.D. & Hamby, I.M.	Antiangiogenic agents. Curr. Opin. Biotec.	Luci 10 544 540 (Dec 1000)			
,		Kions, W. D. & Hamby, J. M.	Andangiogenic agents. Curr. Opin. Biolect	nnoi. 10, 344-349 (Dec. 1999).			
ċ	BU						
				al mapping and radionuclide perfusion imaging for			
	BV	detection of myocardial viabil	ity. <i>Circulation</i> 98, 1837-1841 (Nov. 1998).				
	<u></u>						
	T	Kornowski, R. et al. Delivery	strategies to achieve therapeutic myocardial	angiogenesis. Circulation 101, 454-458 (Feb. 2000).			
	BW			•			
		I aham R I et al Introperios	rdial delivery of fibroblact grouth factor 2 :-	nduces neovascularization in a porcine model of			
	DV		J. Pharmacol. Exp. Ther. 292, 795-802 (Feb.				
	BX		2	. 			

_				1		Sheet Page 4 of 6				
,		TION	DISCLOSURE CITATION	Docket Number (Optional) CIBT-P01-119	Application Number 09/883,848	를 알 그				
			APPLICATION Il sheets if necessary)	Applicant Ling et al.		Y S				
	(00	<i>5</i>	is circuit if moccessury)	Filing Date	Group Art Unit					
21	2 E		I andau C et al Intrangricar	June 18, 2001 dial basic fibroblast growth factor induces m	1646	no All of chronic				
	3	BY	ischemia. Am. Heart J. 129, 9		yocardiai angrogenesis in a raoon in	not change 1				
SEP P	THE STATE OF THE S	BZ	Lazarous, D. F. et al. Compar Coronary Collateral Developm	rative Effects of Basic Fibroblast Growth Fac nent and the Arterial Response to Injury. Cit	ctor and Vascular Endothelial Grow rculation 94, 1074-1082 (Sept. 1996	th Rector on				
(T	ADEM	-	Lemire J M et al. Character	ization of cloned aortic smooth muscle cells	from young rats. Am. J. Pathol. 14	4. 1068-1081				
	V	CA	(1994).							
		СВ	Litingtung, Y. et al. Sonic he	dgehog is essential to foregut development.	Nat. Genet. 20, 58-61 (1998).					
		СС	MaGovern C. J. et al. Regional angiogenesis induced in nonischemic tissue by an adenoviral vector expressing vascular endothelial growth factor. <i>Hum. Gene. Ther.</i> 8, 215-227 (20 Jan. 1997).							
		CD		Figure goes a long way: Therapeutic angiogenes A. Circulation 94, 3062-3064 (15 Dec. 1996)		dothelial growth				
		CE		of vascular endothelial growth factor from an mice. <i>Circ. Res.</i> 76, 161-167 (Feb. 1995).	a defective herpes simplex virus typ	e l amplicon				
		CF	Motoyama, J. et al. Overlapp 81-84 (Nov. 1998).	ing and non-overlapping Ptch2 expression w	ith Shh during mouse embryogenes	is. Mech. Dev. 78,				
		CG	Murone, M. et al. Hedgehog	signal transduction: from flies to vertebrates.	Exp. Cell Res. 253, 25-33 (25 Nov	7. 1999).				
1		СН	Murone, M. et al. Sonic hedg	ehog signaling by the patched smoothened re	eceptor complex. Curr. Biol. 9, 76-	84 (28 Jan. 1996).				
		CI		vascular endothelial cell growth factor recept athol. 156, 697-707 (Feb. 2000).	or signaling is sufficient to complet	ely prevent retinal				
		CJ	Parmantier, E. et al. Schwanr 713-724 (1999).	n cell-derived Desert hedgehog controls the d	levelopment of peripheral nerve she	aths. Neuron 23,				
	-	СК	Passaniti, A. et al. Methods in Antiangiogenic Agents Using 528 (1992).	n Laboratory Investigation: A Simple, Quant Reconstituted Basement Membrane, Hepari	itative Method for Assessing Angio n, and Fibroblast Growth Factor. La	genesis and ab. Invest. 67, 519-				
	•	CL	Peacock, D. J. et al. A Novel 1995).	Angiogenesis Inhibitor Suppresses Rat Adju	vant Arthritis. Cell Immunol. 160,	178-184 (Feb.				
		СМ	Pearlman, J. D. Magnetic res 1085-1089 (Oct. 1995).	onance mapping demonstrates benefits of VE	EGF-induced myocardial angiogene	sis. Nat. Med. 1,				
-		CN	Pearse, R. V. II et al. Vertebr regulators. Dev. Biol. 212, 32	ate homologs of Drosophila suppressor of fu 3-336 (15 Aug. 1999).	sed interact with the gli family of tr	anscriptional				
-		со	Pepinsky, R. B. et al. Identifi 14045 (1998).	cation of a palmitic acid-modified form of h	ıman Sonic hedgehog. J. Biol. Che	m. 273, 14037-				

				Sheet Page 5 of 6			
Form PTO/S			Docket Number (Optional)	Application Number			
		DISCLOSURE CITATION	CIBT-P01-119	09/883,848			
		APPLICATION	Applicant				
(Us	e severa	al sheets if necessary)	Ling et al.				
SIPE			Filing Date	Group Art Unit			
10115	6	Denimalar D. D. et al. Manni	June 18, 2001	1646 P 10006 100			
		Pepinsky, R. B. et al. Mappi	ng sonic neagenog-receptor interactions	by steric interference. J. Biol. Chem. 275 1099 100			
SEP 2 0 2007	ep	(2000).		Ÿ Ÿ Ö			
SEP 2 U ZOU							
	E!	Perrimon, N. Hedgehog and	l beyond. Cell 80, 517-520 (1995).				
By and	CQ.			1600			
PADENA	1			7E002			
		Pola et al. The morphogen S	onic hedgehog is an indirect angiogenic	agent upregulating two families of anging nic growth			
_	CR	factors. Nat. Med. 7, 706-71					
•							
		Rivard, A. & Isner, J. M. Angiogenesis and vasculogenesis in treatment of cardiovascular disease. <i>Mol. Med.</i> 4, 429-440 (Jul					
	cs	1998).	Brogenesis and vascurogenesis in a caus	icht of our diovascular discusse. With Wich. 4, 125-440 (Jul			
	LS	1330).					
	ļ	<u> </u>					
		Rivard, A. et al. Age-depend	lent impairment of angiogenesis. Circui	lation 99, 111-120 (Jan. 1999).			
	CT						
		•		pulmonary arterial smooth muscle cell line that maintains			
	CU	differentiated properties thro	ugh multiple subcultures. Circulation 8	6, 1977-1986 (1992).			
	1						
	1	Sato, N. et al. Induction of the	ne hair growth phase in postnatal mice b	y localized transient expression of Sonic hedgehog. J. Clin.			
	cv	Invest. 104, 855-864 (Oct. 19					
	 	Schratzberger P et al Favor	rable effect of VEGF gene transfer on is	chemic peripheral neuropathy. Nat. Med. 6, 405-413			
		(April 2000).	date effect of VEGI gene dansier of is	onomic peripheral near epacity. Nan 1120a. 0, 105 115			
	cw	(4					
				all angiogenesis in dogs with mature collateral vessels. J.			
1	CX	Am. Coll. Cardiol. 29, 1102-	l 106 (April 1997).				
		StJacques, B. et al. Sonic h	edgehog signaling is essential for hair d	evelopment. Curr. Biol. 8, 1058-1068 (1998).			
	CY						
		1					
<u> </u>		St -Jacques B et al Indian I	hedgehog signaling regulates proliferation	on and differentiation of chondrocytes and is essential for			
	cz	bone formation. Genes Dev.		in the differentiation of enough or year and is essential for			
	CZ		,				
		Stars D. M. at al. Character	:4:	J			
		Gli. J. Cell. Sci. 112, 4437-4		d, a negative regulator of the zinc-finger transcription factor			
	DA	Gii. J. Ceii. Sci. 112, 4437-4	448 (DCC. 1999).				
				rabbits treated with an alphavbeta3 antagonist. J. Clin.			
•	DB	Invest. 103, 47-54 (Jan. 1999)).				
		Takeshita, S. et al. Intramuso	cular administration of vascular endothe	lial growth factor induces dose-dependent collateral artery			
•	DC	augmentation in a rabbit mod	lel of chronic limb ischemia. Circulatio	n 90, 228-234 (Nov. 1994).			
-							
	+	Takeshita, S. et al. Theraneu	tic angiogenesis following arterial gene	transfer of vascular endothelial growth factor in a rabbit			
	DD		Biochem. Biophys. Res. Comm. 227, 6				
	┼	Toylor F D at al Enhanced	notonov of human sonia hadaah b t	hydrophobic modification. <i>Biochemistry</i> 10, 4359-4371			
	DE	(April 2001).	. potency of numeri some neagenog by n	iyurophoole mounication. Dioenemistry 10, 4339-43/1			
	DE	(April 2001).					
	<u> </u>	m .m . n n					
				ponents in the developing and adult rat nervous system.			
	DF	Eur. J. Neurosci. 11, 3199-32	214 (Sept. 1999).				

		·····		Sheet Page					
orm PTO/SB/08		Docket Number (Optional)	Application Number	E C					
	N DISCLOSURE CITATION	CIBT-P01-119	09/883,848						
	N APPLICATION	Applicant		S					
	eral sheets if necessary)	Ling et al.	Crown Art Unit	<u> </u>					
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- TE	Traiffort F et al Regional I	Distribution of Sonic Hedgehog, patched, and sr							
n was who			noonened may, in the assay.	65 ~					
0 5005 PDG	, ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,			2002					
	Harris E. E. Davis Charles		i	iol. 266, 158					
ADEMARKS DH	1	growth factor enhances myocardial collateral fl	ow in a cartine model. Am. J. P	E 200, 138					
	Vale, P.R. et al. Catheter-bas	ed myocardial gene transfer utilizing nonfluoro	scopic electromechanical left v	entricular mappi					
i DI	114 0110 11104040		F						
•	·								
	Valentini R P et al Post-tra	anslational Processing and Renal Expression of	Mouse Indian Hedgehoo / R	iol Chem 272					
DJ	0444 0453 (30.34 1.1004)	instantial i rocessing and iteration expression of	Wouse maint Heagenog. J. D.	101. Catem. 272,					
נט		•							
	W-1-1 D A Australia		1000)						
		and arthritis. Rheumatology 38, 103-112 (Feb.	1999).						
DK									
									
	1	al disruption of hedgehog signaling pathway de	fines its critical role in hair dev	elopment and					
DL	regeneration. J. Invest. Derm	regeneration. J. Invest. Dermatol. 114, 901-908 (May 2000).							
		Wood, J. M. et al. PTK787/ZK 222584, a novel and potent inhibitor of vascular endothelial growth factor receptor tyrosine							
DN		kinases, impairs vascular endothelial growth factor-induced responses and tumor growth after oral administration. <i>Cancer Res.</i> 60, 2178-2189 (April 2000).							
	60, 21/8-2189 (April 2000).								
		sculogenesis, angiogenesis, and growth factors	: ephrins enter the fray at the bo	rder. Cell 93, 60					
DN	1 664 (29 May 1998).								
	Yanagisawa-Miwa, A. et al.	Salvage of infracted myocardium by angiogenic	c action of basic fibroblast grow	th factor. Scien					
DC	257, 1401-1403 (4 Sept. 1992).								
	Zhu Z & Witte I Inhibitio	n of tumor growth and metastasis by targeting t	himor-associated annionenesis i	with antagonists					
DP		othelial growth factor. Invest. New Drugs 17, 1		with antagomsts					
DP			20 212 (1222).						
			<u></u>	, · · <u> </u>					
		DATE CONS	SIDERED						
AMINER		l l							
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		or not citation is in conformance with MPEP §							

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